Ophthalmologic Findings in a Premature Infant leading to a Zika Diagnosis during the COVID-19 Pandemic: A Case Report

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We report on the first case of congenital Zika syndrome to be identified during the COVID-19 pandemic in Puerto Rico. The Zika virus (ZIKV) infection was first seen in Puerto Rico in December 2015. It is a flavivirus with vertical transmission, spreading from infected mothers to their fetuses and having a broad spectrum of clinical manifestations, of which microcephaly is the most worrisome. In Puerto Rico, routine ZIKV screening during pregnancy was implemented in October 2016. However, this practice has become less frequent over time. Nevertheless, the transmission of ZIKV continues, so it is important to ensure routine ZIKV screening in endemic regions, such as Puerto Rico.

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The Zika virus (ZIKV) is a flavivirus that is best known for having caused an outbreak in 2016. It is transmitted via the Aedes mosquito, specifically Ae. albopictus and Ae. aegypti, the latter being the most common species of mosquito in Puerto Rico. The presence of these vectors predisposes the island's population to infections, including ZIKV. Pregnant women infected with ZIKV are at risk of vertically transmitting the virus to the fetus. When exposed to ZIKV in the uterus, fetuses are at risk of developing congenital Zika syndrome (CZS). This syndrome causes diverse malformations in the fetus that include cranial, brain, limb, and ophthalmologic abnormalities, among others (1). Of these clinical manifestations, it was the presence of microcephaly that usually led towards ZIKV screening in affected patients. However, it was later demonstrated that infants exposed to ZIKV in utero had other manifestations, even in the absence of microcephaly. When it comes to ocular anomalies, ZIKV causes a wide range of different ophthalmologic changes that may be present in up to 55% of affected infants (2). The most common ocular findings are pigment mottling and chorioretinal atrophy in the macular region. This case demonstrates how an incidental finding during a routine ophthalmologic screening led to the diagnosis of CZS. To our knowledge, this was—and remains—the first case of CZS diagnosed in Puerto Rico during the COVID-19 pandemic.

Case Report

The patient was a premature female, adequate (in terms of her size) for gestational age, born by cesarean section at 32 weeks of gestational age due to a preterm premature rupture of membranes (PPROM) at 21 days before term. Her mother was a 20-year-old healthy woman (gravida 2, para 1) who had had good prenatal care. Prenatal serologic tests, including a VDRL, a hepatitis B, and an HIV test, were all non-reactive, and her group B Streptococcus culture was negative. She remained afebrile during the whole pregnancy, without signs or symptoms of infection. Perinatal interventions included the administration of antenatal steroids for fetal lung maturation and intravenous antibiotics to reduce the risk of infection due to the premature rupture of membranes that occurred. No resuscitation measures were needed at birth, and the patient received Apgar scores of 7 and 9 at 1 and 5 minutes, respectively. Her anthropomorphic measures were as follows: weight, 1380 grams (10th – 25th percentiles), length, 42 cm (25th – 50th percentiles), and head circumference, 27.5 cm (10th – 25th percentiles). The patient was admitted to the neonatal intensive care unit (NICU) because of her prematurity and very low birth weight. Her physical examination was unremarkable, and her vital signs were adequate for her age. The typical manifestations of CZS, such as severe microcephaly, subcortical calcifications, congenital contractures, and marked hypertonia, were not present at birth. Upon ophthalmologic screening for retinopathy of prematurity (ROP), the following signs were seen: a vertically oval, optic nerve head cupping, diffuse perifoveal reflex, and a yellow oval 3-disc diameters in area temporal and inferior to the fovea lesion obscured the choroid vascular pattern. Overlying retinal vessels were visible and traceable (Figure 1). The findings were compatible with focal choroiditis of an infectious or toxic origin, and based on them, the ophthalmology service recommended that ZIKV screening be performed. A further evaluation (via blood tests) for intrauterine or perinatal exposure to viruses (including toxoplasmosis, rubella, cytomegalovirus, herpes simplex I, and Zika) was performed. Of these blood tests, only anti-ZIKV immunoglobulin M came back positive. Her subsequent head circumference was 29.5 cm (below the 5th percentile) at 36 weeks postnatal age, which was worrisome

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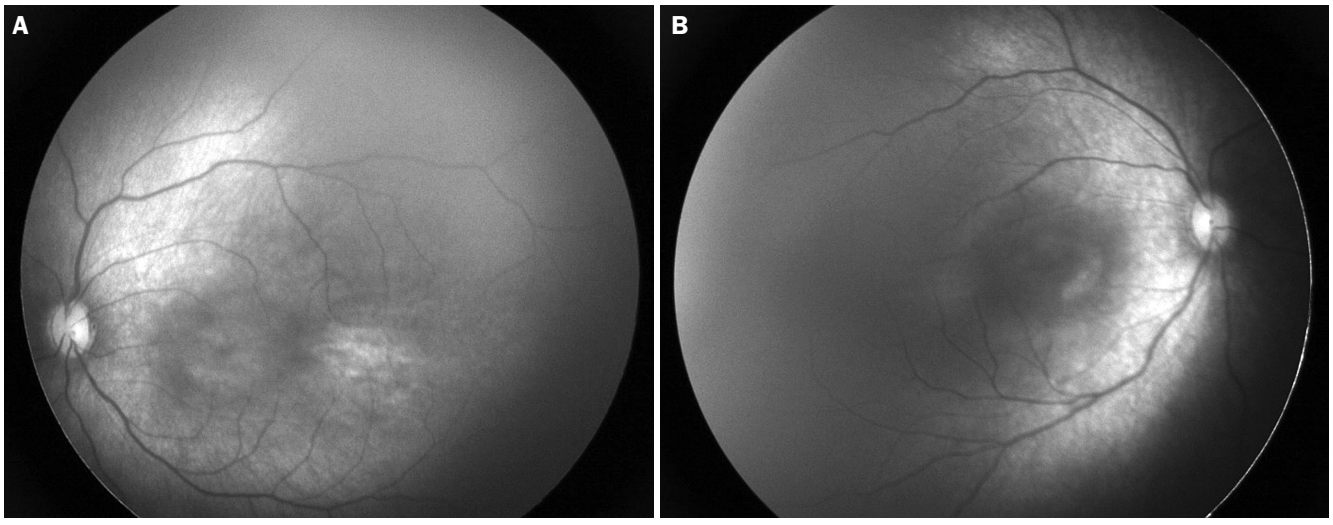
in that the measure is an indication of late microcephaly. During her hospital course in the NICU, the patient developed oropharyngeal dysphagia (OPD), another characteristic described in Zika-exposed patients (3). The rest of her stay was routine. The patient was discharged home with scheduled follow-ups at the specialized Zika clinics, neonatal/pediatric high-risk clinic, and pediatric ophthalmology clinic, all at the University of Puerto Rico Medical Sciences Campus.

Discussion

The Centers for Disease Control and Prevention defined CZS as a distinct pattern of birth defects and disabilities that are caused by the ZIKV infection during pregnancy. These are severe microcephaly, decreased brain tissue with subcortical calcifications, macular scarring and focal retinal pigmentary mottling, congenital contractures, and hypertonia (4). Of these, our patient presented focal choroiditis and late-onset microcephaly. Ventura et al. were the first to report specific retinal changes in association with CZS in Brazilian newborns during the 2016 Zika epidemic (5–9). Moreover, in this case, it was the retinal changes incidentally found during routine screening for ROP that prompted a further workup for congenital infections and eventually led to the diagnosis of CZS. Another important neurological finding in this patient was OPD. As confirmed by Oliveira et al. (2021), OPD is another feature of CZS, especially in patients with associated microcephaly (10). The late-onset microcephaly evidenced in our patient at 36 weeks of gestational age further supports the CZS diagnosis, as it is known that some CZS infants who do not meet the criteria for microcephaly at birth, do so later (11). Nevertheless, to our knowledge, this is the first case in Puerto Rico to be diagnosed this way and the first to be reported during the COVID-19 pandemic.

The ZIKV infection was first identified in Puerto Rico in December 2015, and its identification was followed by an immediate and dramatic increase of cases (14). This promoted the establishment of new public health protocols, including routine ZIKV screening during pregnancy, resulting in a decline in the number of ZIKV cases. As time went by, the administrative orders changed, now establishing that only symptomatic gravidas should undergo screening for ZIKV. Nevertheless, the transmission of ZIKV continues. In 2016 in Puerto Rico and the other US territories, 36,367 cases of Zika were reported; at that time, routine testing for Zika was in place. Now that there is no such routine testing, the number of reported cases has fallen to 57 (for 2020), leading to the question, are there, in fact, fewer Zika cases, or is Zika as prevalent as ever, with the cases simply not being reported. (4). A high level of suspicion is needed to identify a high-risk patient, as that individual may not fulfill the diagnostic criteria at birth. Specifically, ophthalmologic evaluation could be a key diagnostic tool when CZS.is suspected and there are no other physical findings (12). In addition, the integration of a multidisciplinary team is required to deal with every aspect of the condition as early as is possible. For example, CZS patients with ocular manifestations are expected to have visual impairment. However, if exposed to early visual rehabilitation, they could develop a functional level of vision (13). Regarding dysphagia, it is a common cause of death in patients with CZS. Infants exposed early to speech therapy are able to strengthen the oropharyngeal muscles and learn to coordinate the swallowing technique. This reduces the need for gastrostomies and other invasive procedures for feeding. In the long term, these patients also have better language development. This demonstrates the importance of continued routine ZIKV screening in endemic regions amidst the COVID-19 pandemic.

Figure 1. (A) Right Eye; (B) Left Eye. Per the retinal image capture system for retinopathy of prematurity screening, the photos show no retinopathy of prematurity. The optic nerve is somewhat small, pea shaped with temporal optic cup; prominent pigmentary changes in central macula; optic nerve head cupping Arteries and nerves are unremarkable. The central macular area has prominent pigmentary changes. There is a large oval temporal to washed-out areas. This phenotype was found to be more frequent in patients with a history of fetal exposure to the Zika virus and in areas in which the infection rate of Zika was highest.



Resumen

Reportamos el primer caso de Síndrome Congénito por el virus del Zika identificado durante la pandemia de COVID-19 en Puerto Rico. El virus del Zika fue identificado por primera vez en Puerto Rico en diciembre del año 2015. Es un flavivirus con transmisión vertical de madres infectadas a sus fetos. Tiene un gran espectro de manifestaciones clínicas de las cuales la microcefalia es la más preocupante. En octubre del año 2016, se implementó en Puerto Rico un tamizaje rutinario del virus del Zika a toda mujer embarazada. Sin embargo, esta medida de control y salud pública ha caído en desuso con el paso del tiempo a pesar de que los casos de infección con el virus de Zika continúan. Con este caso demostramos la importancia de mantener el tamizaje rutinario del virus del Zika en regiones endémicas como Puerto Rico.

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